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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,154	10/04/2001	Toyohide Shinkawa	249-201	9598

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,154	SHINKAWA ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,8-20 and 22-26* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☒ Claim(s) *1,5,10 and 11* is/are allowed.

6)☒ Claim(s) *8,9,12-17 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment of 0502/05 has been entered. Claims 1,5,8-20 and 22-26 are pending. Claims 1,5,8-17 and 22-26 are under examination.

The amendment has overcome previously stated issues as follows:

The objection to claim 4 under 37 CFR 1.75.

The rejection of claims 1-17 under 35 USC 112, 2nd paragraph.

The rejection of claims 1-3,6-7 and 15-17 under 35 USC 112, 1st paragraph.

The prior art rejection under 102 based upon Dobre et al.

The prior art rejection under 102 based upon Peng et al.

The prior art rejection under 102 based upon Boyle et al.

The prior art rejection under 102 based upon Adams et al.

The prior art rejection under 102 based upon Bridonneau et al.

Applicant's amendment has necessitated the following new ground(s) of rejection.

Claims 8-9, 12-17 and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of independent claims 8-9, 12-13 and 22, recitation of "eluting the antibody composition from the column with an eluent to obtain an adsorbed fraction" is unclear, because what has been eluted is no longer "adsorbed". It is suggested that applicant recite –eluted fraction—instead of "adsorbed fraction" in this step and in the following step of each claim. See Example 2 for support.

Claims 24-25 each recite "the lectin is bound" while base claims 9 and 11 recite the "lectin is immobilized". Consistent terminology is required.

Claims 13 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: in the "applying" step, applicant has failed to state that this is "to adsorb the antibody composition to the column". Note such a parallel recitation in the "applying" step of claim 12, which likewise recovers an adsorbed fraction.

Claims 12, 15-17 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 12 and 26 recite new matter by requiring the carrier for hydrophobic chromatography to be a synthetic resin. The examiner finds no use of the term "synthetic resin" in the section at pages 20-21 pertaining to hydrophobic chromatography.

Upon further consideration the following grounds of rejection are newly stated.

Claims 12-14,16-17 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Goheen et al (J. Chromat., 326, 235, 1985).

Goheen et al separate whole human serum on an HPLC column of Bio-Gel TSK-phenyl-5PW (deemed to be the same as used in instant Ex. 4; in any event this is a resinous material, as disclosed by the reference at p 238). A second eluted peak contains immunoglobulin (p 237).

Goheen et al disclose nothing about the galactose content of their purified immunoglobulin; however, Applicant's claim 12 is so broad that it encompasses exactly what Goheen et al did. Any human serum would have a collection of immunoglobulins which are heterogeneous in their carbohydrate content; thus at least some immunoglobulins in the serum would have some degree of galactose as a constituent of their carbohydrate content; this is all that is necessary to satisfy the conditions set forth in the claim preamble. The rest of claim 12 says nothing about what eluted fraction contains or does not contain gal, and it says nothing about the conditions of elution; thus what Goheen et al recovered as their second fraction is consistent with the instant claim language.

Regarding claim13, applicant has disclosed (p 24) that gal content is associated with CDC and ADCC activity. Thus it is taken that the method of Goheen et al would have inherently provided a serum immunoglobulin preparation having increased CDC and ADCC activities.

Regarding dependent claim(s) 16-17, any preparation of normal human serum would inherently contain IgG, including IgG1.

Claims 13 and 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Danielsson et al.

Danielson et al adsorb and then elute various monoclonal antibody preparations on Alkyl Sepharose HR (p 80, col. 2). Claim 13 says nothing about what eluted fraction contains or does not contain the CDC/ADCC activity, and it says nothing about the conditions of elution; thus what Danielsson et al recovered as their eluted fraction is consistent with the instant claim language. Absent evidence to the contrary it is taken that the hydrophobic interaction chromatography procedure of Danielsson et al would have inherently provide for a preparation

with increased CDC/ADCC activity, which would be a desired property in the case of antibodies against the tumor antigen CEA (Table 1).

Regarding claims 16-17, these anti CEA antibodies are IgG1.

Claims 12-13, 16-17 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Shadle et al (5,429,746).

Shadle et al show a process for purification of human IgG that includes HIC (col., line 26-col. 8, line 3). Organic resins are taught as a carrier/support at col.6, lines 48-49. Phenyl ligands are taught at col.6,lines 50-52. While the reference does not refer to gal content or to ADCC/CDC properties of the IgG obtained, it has been noted supra (rejection over Goheen et al) that the claim language is broad enough to encompass merely the separation steps by HIC per se; also the product obtained is considered to have the properties recited in the preambles of claims 12-13,absent evidence to the contrary.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rinderknecht (WO 96/33208) in light of Turner and view of Adams et al (WO99/10494 or US 6,342,220).

Rinderknecht et al teach (page 12) separation of antibody products via affinity chromatography on protein A attached to an agarose carrier/matrix, or attached to a poly(styrenedivinyl) benzene carrier/matrix (protein A is a bacterial lectin, as evidenced by

Turner èt al at coI.3, lines 50-56). Rinderknecht et al teach the latter carrier as being an advantageous carrier for achieving a good flow rate and for and providing shorter processing times than with agarose. Poly(styrenedivinyl) benzene is a synthetic resin polymer. Rinderknecht et al teach that Protein A selects for certain classes of antibody (a "desired property"). Rinderknecht et al do not give the details of how to affinity purify antibody on Protein A; however, this process is typically done such that one adsorbs antibody to Protein A attached to a carrier, then washes the carrier, and then elutes the desired antibody from the Protein A attached to the carrier. See Adams et al at col.51, lines 56+ showing such a process using a Protein A Sepharose column (Note Sepharose is an agarose based product). Thus using protein A attached to a poly(styrenedivinyl) benzene carrier/matrix, taught by Rinderknecht et al in lieu of the Sepharose carrier of Adams et al would have been obvious, in order to gain the advantage of a faster flow rate. Such a process would be consistent with instant claim 22, which is drawn to a process for recovering an adsorbed, and presumably eluted (see 112, 2nd supra), fraction.

Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dobre et al in view of Rinderknecht et al.

Dobre et al show the fractionation of rabbit IgG on a Con A-Sepharose 4 B column. The Con-A retained fraction has a higher affinity for Fc receptor bearing macrophages, than does the unfractionated lgG. This affinity for macrophages is a "desired property" since macrophages with antibody bound to Fc receptors can participate in an activity such as ADCC - e.g. see specification pages 16-17. From the above, all aspects of instant claims 22-23, which are drawn to a process for recovering an adsorbed, and presumably eluted (see 112, 2nd supra), fraction are shown but for the use of a carrier that is a synthetic resin polymer, rather than Sepharose.

Rinderknecht et al teach (page 12) separation of antibody products via affinity chromatography on protein A attached to a Sepharose carrier/matrix, or attached to a poly(styrenedivinyl) benzene carrier/matrix. Rinderknecht et al teach the latter carrier as being an advantageous carrier for achieving a good flow rate. Poly(styrenedivinyl) benzene is a synthetic resin polymer. One of skill would have fully expected the teachings of Rinderknecht to also apply for the case in which the active affinity receptor is a lectin other than Protein A (e.g. a lectin such as the Con-A of Dobre et al), since the flow rate depends on the nature of the carrier/matrix rather than upon the nature of the receptor/lectin attached thereto. Thus conducting the method of Dobre et al with the use of a synthetic resin column, rather than a Sepharose column, would have been obvious, in order to gain the advantage of a faster flow rate.

Claims 12-13, 15 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shadle et al in view of Rinderknecht et al.

Shadle et al were cited supra against claims 12-13, with respect to purification of immunoglobulins via HIC. They also teach purification of immunoglobulins via Protein-A Sepharose chromatography (col.8,lines 25+). It has been noted supra that Rinderknecht et al teach that a poly(styrenedivinyl) benzene carrier/matrix is an advantageous carrier for achieving a good flow rate. Thus it would have been obvious to use a poly(styrenedivinyl) benzene carrier/matrix in any Protein A purification method taught by Shadle et al; claim 22 would thus have been obvious.

Regarding claim 15, Shadle et al teach combining HIC and Protein A purification methods (col.7,line 64-col. 8,line 33).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644